REDACTED – PUBLIC VERSION

IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

SMITH KLINE & FRENCH LABORATORIES, LTD, AND SMITHKLINE BEECHAM CORP., d/b/a GLAXOSMITHKLINE, Plaintiffs, v. TEVA PHARMACEUTICALS USA, INC., Defendant.	Civil Action No. 05-197 GMS **FILED UNDER SEAL**

DEFENDANT TEVA PHARMACEUTICALS USA, INC.'S POST-TRIAL BRIEF ON THE DEFENSE OF INEQUITABLE CONDUCT

John W. Shaw (No. 3362)
Monté T. Squire (No. 4764)
YOUNG CONAWAY STARGATT & TAYLOR, LLP
The Brandywine Building
1000 West Street, 17th Floor
Wilmington, DE 19801
Telephone: (302) 571-6600
msquire@ycst.com

Attorneys for Defendant Teva Pharmaceuticals USA, Inc.

Of Counsel
Daniel F. Attridge, P.C.
Edward C. Donovan
Andrew B. Kay
Charanjit Brahma
Corey J. Manley
Valerie L. Gutmann
KIRKLAND & ELLIS LLP
655 Fifteenth St., N.W.
Suite 1200
Washington, D.C. 20005
Telephone: (202) 879-5000

Dated: February 7, 2007

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This Court should find that Dr. David A. A. Owen and his representatives from GSK engaged in inequitable conduct during the prosecution of U.S Patent No. 4,824,860 ("the '860 patent")[1] rendering the patent unenforceable. The '860 patent asserted rights over subject matter the applicants knew the named inventor did not invent and distinguished the prior art based on arguments the applicants knew to be false. While GSK contends this is somehow standard patent prosecution practice, the law unambiguously says otherwise. The record clearly shows two separate instances of inequitable conduct committed by Dr. Owen and/or representatives of GSK, each of which is enough to render the '860 patent unenforceable.

Dr. Owen and his representatives made false and misleading arguments to the Patent Office to obtain patent protection for a method of using known compounds to treat Parkinson's disease. *See Hoffmann-LaRoche, Inc. v. Promega Corp.*, 323 F.3d 1354, 1363 (Fed. Cir. 2003) (affirming inequitable conduct based on misrepresentations in patent specification). ***First***, Dr. Owen and his representatives falsely declared to the United States Patent and Trademark Office ("USPTO") that Dr. Owen alone was the sole inventor of the claimed subject matter of the '860 patent. *See PerSeptive Biosys., Inc. v. Pharmacia Biotech Inc.*, 225 F.3d 1315, 1320 (Fed. Cir. 2000) (affirming inequitable conduct based on "misrepresentations, omissions and half-truths to the PTO" regarding inventorship). Indeed, accepting as true the arguments and expert testimony that GSK presented at trial on the issue of invalidity, there was no basis to claim Dr. Owen was the sole inventor of the use of ropinirole hydrochloride as an anti-Parkinson's agent because Dr. Owen's claimed hypothesis was simply "a mere hope or expectation" that was insufficient for conception. *See Amax Fly Ash Corp. v. United States*, 514 F.2d 1041, 1047 (Ct. Cl. 1975). To

[1] U.S. Patent No. 4,824,860 has been entered into evidence as PTX 35, but for ease of reference, is referred to as "the '860 patent" herein.

be sure, tests showing the anti-Parkinson's effects of ropinirole described in the '860 patent, but—unknown to the USPTO—***not a single one*** was selected, performed, or interpreted by Dr. Owen or under his direction. (Owen Dep. Tr. at 110:10-111:3.)[2] The researchers who performed this work were never identified to the USPTO, nor were their written reports that were the origin of the patent's data ever produced to the USPTO. *See Hoffman-LaRoche*, 323 F.3d at 1363-64 (misrepresentation of test performed in specification is grounds for inequitable conduct).

Equally problematic in this respect is that claim 1 of the '860 patent is not limited to the use of ropinirole hydrochloride for treating Parkinson's disease. Rather, it also claims the use of ***749 other compounds*** as anti-Parkinson's drugs. But Dr. Owen neither conceived nor considered using any of these other compounds, and none of the other 749 compounds were tested for anti-Parkinson's effects. *See In re Mantell*, 454 F.2d 1398, 1402 (C.C.P.A. 1972) (conception of species insufficient as conception of genus unless there exists "a basis for a reasonable inference of possession of the generic invention"); *Bosies v. Benedict*, 27 F.3d 539, 542-43 (Fed. Cir. 1994) (no conception of genus shown without evidence that inventor himself had definite idea of all compounds within the genus). To the contrary, Dr. Owen testified that he would not have expected the other compounds to work absent the type of testing (performed by others) described in the '860 patent with respect to ropinirole. Dr. Owen categorically disclaimed originating the generic chemical formula in claim 1 and confirmed that he never thought to use any compound other than ropinirole as a treatment for Parkinson's disease. Yet in the declaration of inventorship he submitted to the USPTO, Dr. Owen swore under penalty of

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2 All exhibits and deposition testimony cited herein can be found in the Appendix attached herewith.

perjury that he was the "sole inventor" of the use of all 750 claimed compounds as a method of treating Parkinson's disease. This sworn statement is false. *See PerSeptive*, 225 F.3d at 1320 (affirming inequitable conduct where named inventors had not discovered invention alone and where "extensive collaboration" with others was not disclosed).

Second, to avoid the prior art, the applicants argued that the known dopamine agonist compounds identified in the '860 patent were understood to be different from the prior art dopamine agonist compounds. In particular, the '860 patent credits Dr. Owen with discovering that the claimed dopamine agonist compounds which the '860 patent admits were already known to act ***"pre-synaptically"***, also acted ***"post-synaptically"***—just like the prior art "post-synaptic" dopamine agonist compounds that were well-known treatments for Parkinson's disease. When confronted with this "pre" versus "post" distinction at his deposition, however, Dr. Owen admitted it was, in his words, an ***"absolute irrelevance."***[3] (Owen Dep. Tr. at 192:13-193:3.) Moreover, GSK's own contemporaneous documents confirm the distinction made in the '860 patent was not even true: the prior art anti-Parkinson's dopamine agonists were known to be pre-synaptic as well as post-synaptic D_2 agonists.

There is no reasonable explanation for the false statements and misleading arguments the applicants made during *ex parte* prosecution of the '860 patent, without which this Court should infer that the applicants acted with the intent to deceive the USPTO. *See Bruno Indep. Living Aids, Inc. v. Acorn Mobility Servs. Ltd.*, 394 F.3d 1348, 1354 (Fed. Cir. 2005) ("Bruno has not proffered a credible explanation for the nondisclosure, and an inference of deceptive intent may fairly be drawn in the absence of such an explanation.") Here, the evidence shows the '860

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3 All emphasis added unless otherwise noted.

patent was an unlawful effort to extend patent protection on ropinirole. For four years GSK researchers—first in the U.S. and later in the U.K.—tried and failed to develop ropinirole and other dopamine agonist drugs as cardiovascular agents under the protection of the earlier-filed U.S. Patent No. 4,452,808 ("the '808 patent")[4]. The only "invention" in the '860 patent is the story told in the patent's specification and claims and Dr. Owen's declaration of inventorship. (DTX 97.) Clear and convincing evidence shows the '860 patent was procured through inequitable conduct to extend GSK's monopoly rights over ropinirole and other compounds beyond the life of the earlier-filed '808 patent.[5]

I. PROCEDURAL BACKGROUND

This is an action for patent infringement brought by GSK against Teva in connection with Teva's filing of an Abbreviated New Drug Application ("ANDA") seeking authorization to market generic ropinirole hydrochloride tablets for treating Parkinson's disease. GSK alleges the ANDA infringes claim 3 of the '860 patent. Teva contends the patent is invalid for obviousness and unenforceable for inequitable conduct.

This Court held a trial to take live witness testimony from December 18 to December 20, 2006. The Court directed the parties to submit the designations for witnesses testifying by deposition after the live witness trial. As explained at the pre-trial conference and at trial, the majority of Teva's case for inequitable conduct is based on the testimony of fact witnesses that

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4 U.S. Patent No. 4,452,808 has been entered into evidence as PTX 13, but for ease of reference, is referred to as "the '808 patent" herein.

5 Proposed Findings of Fact and Conclusions of Law on Defendant Teva Pharmaceutical USA, Inc.'s Defense and Counterclaim of Inequitable Conduct are included behind Tab 1 of the attached appendix.

are not under Teva's control and that GSK elected not to bring to trial. As a result, little evidence on the defense of inequitable conduct was presented by live testimony.

Significantly, while the inequitable conduct witnesses were not under Teva's control, they ***were***, for the most part, under GSK's control. For example, all of the following witnesses had key roles in the development of ropinirole hydrochloride and its corresponding patent protection and are either current GSK employees or paid GSK consultants for purposes of this litigation:

- Dr. David Owen, the inventor of the '860 patent, who was a former GSK employee that GSK retained as a consultant for this litigation and was represented by GSK counsel at his deposition (Owen Dep. Tr. at 17:10-18:4);
- Dr. Carol Harvey, the head of the ropinirole project during Dr. Owen's brief involvement, who is a present GSK employee and was represented by GSK at her deposition (Harvey Dep. Tr. at 9:18-20; 16:12-16);
- Mr. Roger Eden, a pharmacologist who worked with Dr. Owen on the ropinirole project, who was a former GSK employee retained as a litigation consultant for purposes of this litigation and represented by GSK counsel at his deposition (Eden Dep. Tr. at 42:13-16; 154:1-5; Owen Dep. Tr. at 106:2-12; DTX 22); and
- Mr. Peter Giddings, a GSK lawyer in the United Kingdom involved in the preparation of the '860 patent, is a present GSK employee and was represented by GSK counsel at his deposition. (Giddings Dep. Tr. at 9:5-11.)

Notably, all of these fact witnesses were not only under GSK's control but also on GSK's "will call" or "may call" trial witness list. GSK, however, elected not to bring them to trial. As a result of GSK's decision, this Court will not hear live testimony from GSK's witnesses attempting to explain away the core issues of Teva's inequitable conduct allegations, including:

- Who prepared the '860 patent application;
- The source of the 749 non-ropinirole compounds in claim 1 of the '860 patent (*see* '860 Patent, col. 6, l. 67-col. 8, 1. 4), and the selection process for their inclusion while other related compounds were excluded;

- How test results from the University of Bradford ended up in a GSK patent application as support for the claimed invention without any disclosure of that other entity's role (*See* '860 Patent, col. 3, l. 40-col. 6, l. 60);

- The source of the dosage information described in the '860 patent (*See* '860 Patent, col. 3, ll. 23-39); and

- Why the '860 patent application asserts a distinction between "pre-synaptic" and "postsynaptic" receptors ('860 patent, col. 1, ll. 48-53) when the named inventor believes that any such distinction is an "absolute irrelevance"? (Owen Dep. Tr. at 192:19-193:3.)

If these witnesses could explain away these questions, presumably they would have done so at trial. And presumably GSK would not have prevented them from testifying about these issues in their depositions by invoking the attorney-client privilege. For example, Dr. Owen was not allowed to testify about any information he may have communicated to GSK's in-house patent department relating to the disclosure of prior art, description of the invention, or involvement of others in its development. (*See, e.g.*, Owen Dep. Tr. at 81:10-16 ("Q. So did you disclose to the patent department whether anyone else worked on the development of ropinirole as a treatment for Parkinson's disease? MS. WIGMORE: I'm going to object and instruct you not to answer. A. I will take my instructions.").)

"Normally, it can be expected that an innocent party will be motivated to try to present convincing reasons for its actions or inaction." *Bruno*, 394 F.3d at 1354-55. Because these witnesses are under GSK's control and not Teva's, this Court may properly infer their testimony would not be exculpatory of GSK, but instead would confirm Teva's evidence of inequitable conduct. *See id.* at 1354-55. When coupled with the fact that these misrepresentations were made in documents deliberately submitted to the USPTO, as opposed to omissions that might be inadvertent, and the USPTO's inability to investigate GSK's assertions regarding inventorship, the record provides clear and convincing evidence of Dr. Owen's and GSK's intent to deceive the USPTO.

II. BACKGROUND

Central to the inequitable conduct in this case is the unexplained disconnect between Dr. Owen's minimal involvement in GSK's ropinirole project and current understanding of the invention and prior compound to the expansive breadth of the '860 patent that bears his name as the sole inventor and the misrepresentations therein.

A. Dr. Owen's Alleged Contribution Is Limited To A "Hypothesis".

Even accepting Dr. Owen's testimony as true, at best his contribution to GSK's ropinirole project was minimal. Dr. Owen is a former pharmacologist at GSK predecessor SmithKlineFrench in England who specialized in cardiovascular drugs. (Owen Dep. Tr. at 54:22-55:8, 127:16-17.) Dr. Owen's involvement in the ropinirole project was limited to the time period from approximately late 1985 (*id.* at 74:8-15) to some time between late 1986 and mid- to late- 1987. (Harvey Dep. Tr. at 81:10-22.) By contrast, GSK's pre-clinical research with ropinirole started in 1982, when the compound was synthesized by Gregory Gallagher. (DTX 45 at GSK-REQ026680.)

Dr. Owen's first involvement with ropinirole came years after the compound was first developed and then tested as a cardiovascular agent. Dr. Owen first became involved in GSK's ropinirole research work when the project was transferred to GSK's facilities in Welwyn, England, after GSK scientists in Philadelphia spent years attempting to develop the drug as a treatment for hypertension. (Owen Dep. Tr. at 42:19-43:2; 54:22-55:8.) In Welwyn, Dr. Owen was for a short period of time the pharmacologist on the project. (*Id.* at 42:19-43:2.) Under Dr. Owen's direction initially were Mr. Roger Eden (Eden Dep. Tr. at 42:7-9) and a technician who worked in Mr. Eden's laboratory, Annette Wright. (Harvey Dep. Tr. at 49:16-22.) By mid- to late-1987, Dr. Owen had dropped out of the ropinirole project entirely. (*Id.* at 81:5-22.)

Dr. Owen's chief responsibility on the ropinirole project during his short tenure was overseeing the work of others in the pharmacology area, notably Mr. Eden. He was not the head of the project. (*Id.* at 16:12-16) (identifying herself as "global project team leader for [ropinirole] from late 1985 until some point in 1988".) And even when he was part of the ropinirole project team, Dr. Owen "delegated a lot of the day-to-day activity to others, and in particular to Roger Eden." (Owen Dep. Tr. at 106:2-12.)

Dr. Owen's claimed inventive contribution to ropinirole was the "hypothesis" that because (1) ropinirole was a known dopamine agonist at D_2 receptors; and (2) ropinirole was known to have central effects; then (3) it may work as an anti-Parkinson's agent like other known centrally acting dopamine agonists. (Owen Dep. Tr. at 114:21-115:15.) Significantly, Dr. Owen did not discover that ropinirole was a D_2 agonist—that was known years before and disclosed in GSK's earlier filed '808 patent ('808 patent, col. 4, ll. 31-34), and it was part of the "message" Dr. Owen received from Philadelphia when the ropinirole project was transferred to the U.K. (Owen Dep. Tr. at 73:9-74:1). Nor did Dr. Owen discover that ropinirole was centrally acting—that was found by, among others, Annette Wright when she ran tests on animals in dosage amounts well less than the amounts disclosed in the '808 patent. (Eden Dep. Tr. at 62:4-8 (Ms. Wright "was the person who first noted that ropinirole appeared to penetrate the central nervous system."); DTX 24 at GSK-REQ000386, 391 (noting observation of "classic stereotyped 'sniffing'").) Indeed, anyone who ran tests in that dosage range saw the central effects of the drug. (Harvey Dep. Tr. at 146:2-20.) And Dr. Owen was certainly not the first to hypothesize that centrally acting dopamine agonists have utility as anti-Parkinson's agents—that correlation is recognized in the '860 patent itself as already established. ('860 patent, col. 1, ll. 48-53; *see also* DTX 375.) So at best, Dr. Owen claims to be the person who applied known facts to a

known scientific relationship and arrived at the hope—or "hypothesis", as Dr. Owen calls it (Owen Dep. Tr. at 135:3-7)—that ropinirole would behave consistently with the known scientific relationship.

Dr. Owen's only other alleged contribution was to communicate his hypothesis to researchers at the University of Bradford, including Professor Brenda Costall, and ask them to test ropinirole for central effects. (*Id.* at 71:10-72:2.) Dr. Owen admitted that he contacted the University of Bradford because they were the "experts" in neuropharmacology and he was not. (*Id.*) University of Bradford selected, ran, and interpreted the tests on ropinirole for potential anti-Parkinson's activity and other central effects. (*Id.* at 110:10-111:3.) The Bradford researchers prepared reports and sent them back to GSK. (Costall Dep. Tr. at 124:15-20.)

Contemporaneous GSK documents credit University of Bradford, not Dr. Owen, for finding the anti-Parkinson's effects of ropinirole.

> Studies of the CNS properties of SK&F 101468 ***conducted at the University of Bradford*** clearly demonstrated potential utility in Parkinson's Disease.

(*See, e.g.*, DTX 100 at GSK-REQ014480; DTX 28 at GSK-REQ013951.) GSK's meeting minutes documented the relationship between GSK and the Bradford researchers. (*See, e.g.*, DTX 98; DTX 100; DTX 101; DTX 102.) Prior to September 1986, when Professor Costall submitted her first report to Dr. Owen that concluded ropinirole had potential anti-Parkinson's applications (DTX 35), all of the entries in GSK's meeting minutes mentioning the University of Bradford researchers state only that they were being asked to broadly investigate the overall CNS effects of ropinirole. (*See, e.g.*, DTX 98; DTX 100; DTX 101; DTX 102.) No specific mention of Parkinson's disease is made. (*See, e.g.*, DTX 98 at GSK-REQ014412 ("Professor Naylor (Bradford) who is an expert on the CNS effects of dopamine-like compounds, will be consulted next week to determine the most appropriate experimental designs for the investigation of the

neurobehavioral effects of SK&F 101468-A."); DTX 101 at GSK-REQ014399 ("Professors Costall and Naylor are being supplied with SK&F 101468 to study its CNS effects."); DTX 102 at GSK-REQ014385 ("Professors Costall and Naylor have been supplied with SK&F 101468-A and are investigating its CNS effects. Post-Meeting Note: A report on the results of these investigations has been received.").)

Only after Dr. Costall's first report was received by Dr. Owen in September 1986 did GSK's meeting minutes begin to discuss the possibility of developing ropinirole as a treatment for Parkinson's disease:

> The possible development of SK&F 101468 for CNS indications was discussed. Studies of the CNS properties of SK&F 101468 conducted at the University of Bradford clearly demonstrated potential utility in Parkinson's Disease... .
>
> The team were in favour of further assessing the potential utility of SK&F 101468 in Parkinson's Disease. ... Further evaluation of the effectiveness of SK&F 101468 in animal models of Parkinson's Disease would be needed to support clinical trials.

(DTX 100 at GSK-REQ014480.)

Similarly, the August 1987 Draft Project Plan and Review Document for the ropinirole project credits the Bradford researchers—not Dr. Owen—with discovering the anti-Parkinson's potential of ropinirole. (DTX 28 at GSK-REQ013951 ("Evaluation of the CNS profile has been carried out in collaboration with the University of Bradford, U.K.; results suggest ***anti-parkinson*** ... activity.").) And the '860 patent itself lists numerous tests and test results showing ropinirole's use as an anti-Parkinson's agent. ('860 patent, col. 3, ll. 59-62, 67-68; col. 4, l. 61-col. 5, l. 6; col. 5, l. 45-col. 6, l. 53.) All of the tests were selected, run, and interpreted by University of Bradford, not Dr. Owen. (Owen Dep. Tr. at 110:10-111:3.) This evidence proves that, at most, Dr. Owen's alleged contribution consisted of his "hypothesis" that ropinirole's CNS effects might include anti-Parkinson's activity, while all of the work that went to forming a

definite and permanent idea that ropinirole could be used to treat Parkinson's disease was done by others without Dr. Owen's direction.

One would search the record in vain for any contemporaneous evidence that it was Dr. Owen who first hypothesized that ropinirole could be used to treat Parkinson's disease. Indeed, Dr. Owen, a trained scientist, could not remember recording his alleged hypothesis in any document, not even a written communication to the University of Bradford researchers. (*Id.* at 65:2-6.)

But the record is replete with evidence of the contributions of others. Unlike Dr. Owen, Annette Wright, who conducted the experiments that led to the discovery of CNS effects, kept a laboratory notebook in which she noted her observations that rats showed "classic stereotyped 'sniffing'" upon administration of ropinirole. (DTX 24 at GSK-REQ000386, 391.) That notebook does not mention Dr. Owen, and was instead witnessed by Mr. Eden. (*Id.* at GSK-REQ000209.) Mr. Eden likewise testified that Annette Wright, not Dr. Owen, explained to him that the observed stereotypy was "an indication that [ropinirole] was getting into the CNS" (Eden Dep. Tr. at 74:20-75:1), and it was Mr. Eden, not Ms. Wright, that informed Dr. Owen of the central effects. (*Id.* at 80:15-19.) Not surprisingly, Mr. Eden does not credit Dr. Owen with discovering that ropinirole had anti-Parkinson's effects. (Eden Dep. Tr. at 94:14-17.)[6]

Likewise, the record details Professor Costall's extensive testing of ropinirole in several animal models, applying her knowledge as an "expert" in CNS pharmacology. (*See* Owen Dep.

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[6] Mr. Eden claims no credit for himself in coming up with the concept of using ropinirole to treat Parkinson's disease, and he has the unique perspective of having worked closely with Dr. Owen, Professor Costall at the University of Bradford, and Ms. Wright. In fact, by the time the Bradford researchers submitted their second set of reports on ropinirole's potential use as an anti-Parkinson's agent, the reports were sent to Mr. Eden, not Dr. Owen. (Costall Dep. Tr. at 124:15-20.)

Tr. at 71:10-72:2.) Notably, at least one experiment that Professor Costall conducted showed exactly the opposite of the observations made by Ms. Wright's observations of "classic stereotyped 'sniffing'" (DTX 24)—one of the two pieces of information that allegedly prompted Dr. Owen to come up with his hypothesis in the first place. As Professor Costall told Dr. Owen in the September 1986 report, ropinirole "failed to cause marked stereotypy in rat or mouse." (DTX 35 at GSK-REQ001030.) After conducting seven different experiments, Professor Costall and the Bradford researchers came to the conclusion that ropinirole had "anti-Parkinson potential (although direct/indirect activity needs to be established)." (DTX 35 at GSK-REQ001054.) But if Dr. Owen is to be believed, Professor Costall's thorough experiments did not advance the ball one iota from the starting point that Dr. Owen had given her—his alleged hypothesis that ropinirole was "a potential treatment for Parkinson's disease." (Owen Dep. Tr. at 114:21-115:15.)

B. The '860 Patent Goes Far Beyond Dr. Owen's Alleged Hypothesis.

While Dr. Owen's tenure on the ropinirole team ended by 1987 at the latest (Harvey Dep. Tr. at 81:10-22; 202:4-16), the '860 patent was not filed in the United States until a year later on May 19, 1988. (*See* '860 patent.) The '860 patent specification begins with a summary of the background knowledge in the field of treatments for Parkinson's disease. (*Id.* at col. 1, ll. 8-44.) It describes the disease and acknowledges the well-known existing treatments for Parkinson's disease, which included L-dopa and "post-synaptic dopamine agonists." (*Id.*) The specification then describes the alleged "invention" in an effort to distinguish those prior art treatments. (*Id.* at col. 1, l. 54-col. 2, l. 3.)

The '860 patent ends with three claims. (*Id.* at col. 6, l. 56-col. 8, l. 14.) All three claims are independent claims and all are directed to "a method of treatment of Parkinson's disease" by administering "an effective non-toxic amount" of a compound. (*Id.*) Claim 1 is directed to the

method of using any of the 750 different compounds described in the specification, claim 2 is limited to the method using ropinirole, and claim 3 is limited to the method using ropinirole hydrochloride. (*Id.*) These claims define the scope of what Dr. Owen and GSK's patent attorneys told the USPTO that Dr. Owen had conceived, but they bear little relation to Dr. Owen's alleged hypothesis.

1. The Alleged Discovery That 750 Pre-Synaptic Compounds Acted Post-Synaptically.

The '860 patent credits Dr. Owen with discovering that a series of compounds, including ropinirole, were not just pre-synaptic dopamine agonists, but also post-synaptic dopamine agonists:

> certain indolone derivatives known in the art as pre-synaptic D_2 agonists having utility as cardiovascular agents [citing European equivalent of the '808 patent], are also post-synaptic D_2-agonists in the brain and hence are expected to have utility in the treatment of Parkinsonism

(*Id.* at col. 1, ll. 48-53.) More specifically, the patent credits Dr. Owen with discovering that 750 different claimed compounds presumably all exhibit "post-synaptic D_2 agonist" activity in the brain. (*See id.*) The compounds are identified by a common structural formula having certain different substituents that may be substituted into the formula. (*Id.* at col. 2, ll. 4-24.)

2. The Disclosure Of "New" Compounds Not In The Prior Art '808 Patent And "New" Properties For Select '808 Patent Compounds.

While the '860 patent cites the earlier '808 patent as the source of the compounds, not all the compounds described in the '860 patent are from the '808 patent. (Trial Tr. at 515:1-10.) Conversely, only a small subset of the thousands of '808 patent compounds are claimed in the '860 patent as having anti-Parkinson's activity. (*Id.*) No explanation is provided—either in the '860 patent or anywhere else in the record—for why some of the '808 patent compounds were

included while others were not. Nor is the logic for including compounds from other sources explained, much less the reason for attributing the inclusion of those compounds to Dr. Owen.

3. Claimed "Effective" Amounts And Supporting Data, Including Animal Testing.

The '860 patent claims "an effective non-toxic amount" for each of the compounds for treating Parkinson's disease. ('860 patent at col. 6, l. 67-col. 7, l. 1.) In support of these claims, the patent specification identifies specific dosage amounts for treating humans suffering from Parkinson's disease:

> The daily dosage regimen for an adult patient may be, for example, an oral dose between 1 mg and 100 mg, preferably between 1 mg and 50 mg, or an intravenous, subcutaneous, or intramuscular dose between 0.1mg and 50 mg, preferably between 0.1mg and 15 mg, of the compound of structure (I) or a pharmaceutically acceptable salt thereof calculated as the free base, the compound being administered 1 to 4 times per day.

(*Id.* at col. 3, ll. 30-39.) The specification also cites animal testing in support of the alleged effective ranges. (*Id.* at col. 5, l. 46-col. 6, l. 33.)

4. Biological Testing In Support Of Anti-Parkinson's Claims.

In support of the assertion that the 750 claimed compounds are useful for treating Parkinson's disease, the patent describes certain "biological data" including 10 different tests that were performed. (*Id.* at col. 3, l. 40.) ***All*** of these tests were performed with a single claimed compound—ropinirole hydrochloride. (*Id.* at col. 3, ll. 42-45.) None of the other 749 compounds were tested. (Owen Dep. Tr. at 131:13-19.) Two of the tests—test nos. 7 and 10—are described as being "a test for anti-Parkinson's activity." ('860 patent, col. 3, ll. 59-62, 67-68; col. 4, l. 61-col. 5, l. 6; col. 5, l. 45-col. 6, l. 53.)

C. The '860 Patent Claims Inactive Compounds.

Not all of the compounds claimed in the '860 patent for the treatment of Parkinson's disease would have been expected to have dopaminergic activity (Trial Tr. at 219:11-220:20), for

good reason—GSK's own testing had shown that at least one of the claimed compounds was dopaminergically inactive. (*Id.* at 556:20-25; 222:12-17; DTX 56.)

Dr. Long specifically pointed to two examples of compounds that he and others in the field would have expected to be inactive as D_2 agonists, but which are nonetheless identified in claim 1 as anti-Parkinson's agents. (Trial Tr. at 219:21-220:8.)

To support his opinion that these compounds were dopaminergically inactive and ineffective in treating Parkinson's disease, Dr. Long cited not only his own work but the work of others experienced in the field. With respect to the compound shown in DDX 11, Dr. Long specifically pointed to the DeMarinis article as showing the compound to be inactive as a D_2 agonist. (*Id.* at 222:12-17.) Neither Dr. Owen nor anyone else at GSK tested these compounds to prove they were dopamine agonists or effective as treatments for Parkinson's disease.

Second, Dr. Long also testified that, based on his own prior research and publications, which showed that D_2 agonist activity was consistently eliminated whenever a dibutyl group was added to the aminoethyl side chain of a potential dopamine agonist, he believed that the compounds identified in claim 1 in which the "R" substituent was a C_4 alkyl would be expected to be dopaminergically inactive. (*Id.* at 226:3-9.)

For the compounds in claim 1 that include a dibutylamino side chain, Dr. Long pointed to his own previous work – a 1978 article (DTX 160) co-authored by Professors Costall and Naylor, the very researchers at the University of Bradford who did all of the pharmacological testing of ropinirole that is described in the '860 patent – to show that the compound would be expected to be inactive as a D_2 agonist. (Trial Tr. 227:12-229:1.) While it might have been "a great discovery" to find that these dibutyl compounds were active as D_2 agonists and effective in

treating Parkinson's disease, GSK has offered absolutely no evidence to suggest that anyone, much less Dr. Owen, ever tested any such compounds for that purpose.

While GSK's chemistry expert, Dr. Bartlett, offered testimony on this topic, he admitted he had no experience working with or researching dopamine agonists and he could not offer any opinions on issues related to pharmacology. (*Id.* at 533:17-19; 543:16-21.) In other words, he was not qualified to speak to whether particular compounds would or would not be active as D_2 agonists or effective as treatments for Parkinson's disease, and this Court should place no weight on Dr. Bartlett's opinions. Notably, however, even Dr. Bartlett acknowledged that GSK's own researchers had characterized at least one compound identified in claim 1 as "inactive" in GSK's standard assay for determining D_2 agonist activity, contrary to Dr. Bartlett's own unsupported opinions. (*Id.* at 556:12-19.) In sum, the evidence showed that some of the compounds identified in claim 1 were dopaminergically inactive and would not be effective to treat Parkinson's disease, and that GSK researchers who worked on the compounds—including Dr. Owen—knew it.

D. Dr. Owen's Testimony Is At Odds With The '860 Patent And His Declaration.

Like all U.S. patents, the application for the '860 patent included an identification of the inventors of the claimed subject matter and a declaration from those named inventors acknowledging their legal duties relating to the legal document being prosecuted in their name. (DTX 19 at GSK-REQ000555-554; DTX 97.) *See* 37 C.F.R. § 1.63. Indeed, in the United States, patents are only issued to inventors, not companies, and the inventors and their representatives owe duties of disclosure and candor to the USPTO. 37 C.F.R. § 1.56.

When the '860 patent application was filed in 1988, Dr. Owen was identified as the sole inventor of all of the claimed subject matter. (DTX 19 at GSK-REQ000539-554.) Those

application claims never materially changed. (*Id.*) In connection with the patent application, Dr. Owen signed and GSK's patent attorneys filed a declaration (DTX 97) swearing under penalty of perjury that Dr. Owen was the ***sole inventor*** of the claimed subject matter and that he had ***reviewed and understood*** the contents of his patent application:

> I believe I am the original, first and sole inventor . . . of the subject matter which is claimed and for which a patent is sought on the invention entitled Medicament the specification of which is attached hereto.
>
> I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

(*Id.*)

Despite having signed this sworn declaration, Dr. Owen's deposition testimony was stunningly at odds with his patent application. Dr. Owen could not recall ever reviewing the patent application. (Owen Dep. Tr. at 31:19-22.) As Dr. Owen readily admitted when he was shown the '860 patent at his deposition, he never considered whether any other compound might be used to treat Parkinson's disease—his sole focus was ropinirole. (*Id.* at 135:3-7.) For example, he did not consider whether even SK&F 89124, the lead compound from which ropinirole was developed and one of the compounds identified in claim 1, could be used as an anti-Parkinson's agent. (*Id.*) Dr. Owen flatly repudiated the notion that he had any involvement with any compound other than ropinirole hydrochloride. (*Id.* at 131:13-19.) "I only ever hypothesized that ropinirole might be useful in treating Parkinson's disease." (*Id.* at 135:6-7.) Dr. Owen did not believe one could have any expectation that the other 749 compounds identified in claim 1 could be used to treat Parkinson's disease absent testing. (*Id.* at 134:1-10.) Moreover, Dr. Owen disavowed any involvement in determining what compounds other than ropinirole should be claimed, and pointed to GSK's patent attorneys as having identified the

other 749 claimed compounds when they prepared his patent application. (*Id.* at 131:20-132:3; 132:5-16.)

Dr. Owen also rejected the notion that there was a distinction between post-synaptic D_2 agonists and pre-synaptic D_2 agonists, calling such a distinction an "absolute irrelevance" (*id.* at 192:13-17; 192:19-193:3), contrary to the arguments made on his behalf in the patent to distinguish the prior art. ('860 patent, col. 1, ll. 48-53.) He similarly rejected the '860 patent's distinction between expected D_2 agonist activity in the brain or at any other part of the body, flatly stating that "[i]f a compound is a D_2 agonist, [he] would expect it to be a D_2 agonist at D_2 receptors regardless of their anatomical location." (Owen Dep. Tr. at 191:19-21.)

The '860 patent also identifies particular dosages of ropinirole. ('860 patent, col. 4, ll. 28-30 ("At doses of 1.0, 10.0 and 100 mg/kg i.p. Compound A caused no dose dependent stereotypies in the mouse or rat ... .").) Dr. Owen explained he never considered any specific dosages (or "effective, nontoxic amounts" as referred to in claim 1) for the treatment of Parkinson's disease. (Owen Dep. Tr. at 216:10-13; 216:15-217:7; 217:13-18; 217:20.) According to Dr. Owen, all of the dosage information in his patent was put in there by people in GSK's patent department without any input from him. (*Id.*)

With respect to the biological tests, as noted above, Dr. Owen did not direct, perform, or interpret a single one described in the '860 patent. The tests and results for anti-Parkinsonism activity described in the '860 patent came directly from the University of Bradford. Dr. Owen candidly acknowledged he would not assume to question the University of Bradford researchers' judgment. (*Id.* at 71:10-72:2.) Yet nowhere in the patent is there any mention of University of Bradford's contribution or any disclosure of the University of Bradford reports that are the basis for the anti-Parkinsonism test data. (*See* '860 patent.)

E. The '860 Patent Creates a False and Misleading Pre- / Post-Synaptic Distinction.

GSK itself has admitted that the '860 patent's characterization of the prior art compounds was at odds with statements in the prior art that was not identified during the prosecution of the '860 patent. (*See* DTX 134.) While the '860 patent says that prior art Parkinson's disease treatments were known to be "post-synaptic" D_2 agonists ('860 patent, col. 1, ll. 36-38), GSK's own prior art article—the DeMarinis article—contradicts that statement (DTX 56). The DeMarinis article describes these same prior art D_2 agonists as ***pre-synaptic*** D_2 agonists. (*Id.*)

To overcome the EPO's rejection, GSK was forced to acknowledge that statements in the European patent application that were identical to the statement in the '860 patent characterizing the prior art treatments for Parkinson's disease were, in fact, incorrect. (DTX 133 at GSK-REQ018298.) Thus, when the misleading distinction between pre-synaptic and post-synaptic D_2 agonists was held up to scrutiny by the EPO, GSK acknowledged that its statements about the prior art dopamine agonists in the '860 patent were false and misleading. The '860 patent had already issued by the time of GSK's acknowledgement, however, at no time did GSK attempt to correct the '860 patent through reissue or otherwise.

Perhaps more importantly, Dr. Owen knew the pre-/post-synaptic distinction drawn in the '860 patent was not relevant to whether ropinirole would be expected to be effective in treating Parkinson's disease. (Owen Dep. Tr. at 191:11-14.) Dr. Owen's understanding was that there was no pharmacological distinction between "pre-" and "post-" synaptic receptors—"[i]f its an agonist for D_2 receptors, it will be an agonist for D_2 receptors, and whether they are presynaptic or postsynaptic is a piece of anatomy, not a piece of pharmacology." (*Id.*) During his deposition, Dr. Owen admitted that this distinction was "an absolute irrelevance." (*Id.* at 192:19-193:3.)

Despite Dr. Owen's and GSK's knowledge that the pre- and post-synaptic distinction was an absolute irrelevance, GSK never notified the USPTO of this irrelevance during the prosecution of the '860 patent or corrected the patent.

F. GSK Failed Or Refused To Identify The Source Of Information In The '860 Patent.

The disparity between the "official" story of conception told by the '860 patent and its prosecution documents and the story now told by Dr. Owen raises the question of what the actual story is. Incredibly, GSK itself claims not to know (Owen Dep. Tr. at 81:10-16; *See* DTX 132; DTX 136; DTX 137; DTX 138), and through extensive assertions of attorney-client privilege it substantially precluded discovery on the subject. (*See* '860 patent; DTX 19 ("'860 Patent Public Prosecution History"); DTX 312 (internal prosecution history).)

The threshold issue remains: who prepared the '860 patent application? Who put in the mystery dosage information? Who determined which of the thousands of "indolone derivatives" in the prior art '808 patent and '944 patent should be included in claim 1 of the '860 patent and who excluded the others? Who "invented" the other compounds included in the '860 patent claim 1 not found in any earlier patent? And who put in the false "post-synaptic" versus "pre-synaptic" distinction? From the '860 patent prosecution history, it appears the '860 patent was prosecuted by a Mr. Suter, a patent attorney with GSK in the United States. (DTX 19.) The application itself claims priority to an earlier UK patent application filed in May 1987. (*See* '860 patent.) GSK claims not to know who prepared the UK application. Regardless, it is clear from his testimony that Dr. Owen was not responsible for those portions of the claimed invention referenced above.

To ascertain the relevant persons involved, Teva served an interrogatory seeking all those persons involved in preparing the application and prosecuting it. In response, GSK represented:

> . . . GSK presently believes that the following individuals had some involvement in drafting the United States patent application for the '808 and '860 patents and communication with the United States Patent and Trademark Office (the "USPTO") during the prosecution of those patents . . . .
>
> ***
>
> The '860 Patent
> - Vincent L. Fabiano
> - Peter J. Giddings, Ph.D.

(DTX 140 at Response to Interrogatory No. 2.)

In response to Teva's Rule 30(b)(6) notice directed to the same subject, GSK represented that it had no further information in response to the topic and thus was unwilling to provide a witness. (May 30, 2006 Ltr. from M. Gordon to C. Brahma at 2 ("We are not aware of any other [*i.e.*, that Mr. Giddings] current GSK employees having any relevant, personal knowledge about the filing or prosecution of the '860 patent.").) Mr. Giddings, a patent attorney in the UK involved in the ropinirole project, subsequently was deposed. However, like Dr. Owen, he claimed to have no recollection of the events despite three days of preparation with GSK's attorneys. (*See, e.g.*, Giddings Dep. Tr. at 58:22-59:4; 59:10-13.) Yet it is abundantly clear—notwithstanding Mr. Giddings' and Dr. Owen's faltering memories—that there was significant legal activity surrounding the preparation and prosecution of the '860 patent application, reflected in many different entries in GSK's privilege logs. (*See* DTX 132; DTX 136; DTX 137; DTX 138.)

At bottom, GSK's inability—whether real or feigned—to identify specific individuals responsible for the preparation and prosecution of the '860 patent cannot be a basis for it to avoid inequitable conduct. That information is solely under GSK's control. Where, as here, the evidence shows false and misleading statements were made in the patent and during its prosecution, GSK cannot rely on evidence from the specific individuals responsible for those

actions—much less speculation about what those witnesses might have said—where GSK alone could provide it and chose to withhold that evidence during discovery. *Tracinda Corp. v. DaimlerChrysler AG*, 362 F. Supp. 2d 487, 513 (D. Del. 2005) ("[t]he attorney client privilege should not be used as both a sword and a shield.")

III. LEGAL STANDARD

The test for inequitable conduct is whether Dr. Owen or anyone substantively involved in prosecuting the '860 patent: (1) "failed to disclose material information" related to the patentability of the claims of the '860 patent in breach of their duty of candor or disclosure, coupled with (2) an intent to mislead the USPTO. *See Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc.*, 326 F.3d 1226, 1233-34 (Fed. Cir. 2003) (citing *Kingsdown Med. Consultants, Ltd. v. Hollister, Inc.*, 863 F.2d 867, 872 (Fed. Cir. 1988) and *FMC Corp. v. Manitowoc Co.*, 835 F.2d 1411, 1415 (Fed. Cir. 1987).) If clear and convincing evidence of a threshold level of materiality and intent is presented, the Court balances "materiality and intent in light of all the circumstances to determine whether the applicant's conduct is so *culpable* that the patent should be held unenforceable." *Ferring B.V. v. Barr Labs., Inc.*, 437 F.3d 1181, 1186 (Fed. Cir.), *cert. denied,* 127 S. Ct. 515 (2006) (emphasis in original). "The more material the conduct, the less evidence of intent will be required in order to find that inequitable conduct has occurred." *PerSeptive,* 225 F.3d at 1319.

Significantly, inequitable conduct as to any portion of a patent makes the entire patent unenforceable. *Praxair, Inc. v. ATMI, Inc.*, 445 F. Supp. 2d 473, 478 (D. Del. 2006) ("If it is established that a patent applicant engaged in inequitable conduct with respect to one claim, then the entire patent application is rendered unenforceable"). While GSK withdrew its assertion that Teva infringed claim 1 of the '860 patent (*see* 6/23/06 Stipulation (D.I. 60) ¶ 1), GSK originally

asserted those claims in this litigation and they remain a part of the '860 patent, as does the taint arising from any inequitable conduct associated with the withdrawn claims.

The duty of candor and disclosure is not limited to just the named inventors and identified attorneys. Rather, anyone substantively involved in the preparation of the patent application or prosecution of the patent owes these duties to the USPTO. *See Molins PLC v. Textron, Inc.*, 48 F.3d 1172, 1178 n.6 (Fed. Cir. 1995) (duties "rest[] on the inventor, on each attorney or agent who prepares or prosecutes an application and on every other individual who is substantively involved in the preparation or prosecution of the application and who is associated with the inventor" or the assignee). Thus, other scientists or attorneys who make contributions to the patent or review materials for prosecution share the same responsibilities and obligations as the named inventor.

The intent necessary to prove inequitable conduct, an equitable defense as opposed to an affirmative claim, is different than—and less than—that for common law fraud or antitrust. *Nobelpharma AB v. Implant Innovations, Inc.*, 141 F.3d 1059, 1070 (Fed. Cir. 1998). Moreover, intent need not be shown by direct evidence. *See Hoffman-LaRoche*, 323 F.3d at 1371 ("Intent, however, is typically proved inferentially, … and a finding of intent does not require a confession from the stand by the inventor or the prosecuting attorney," citing *Molins, PLC*, 48 F.3d at 1180; *Merck & Co. v. Danbury Pharmacal, Inc.*, 873 F.2d 1418, 1422 (Fed. Cir. 1989)). Rather, "this element of inequitable conduct must generally be inferred from the facts and circumstances surrounding the applicant's overall conduct." *Paragon Podiatry Lab., Inc. v. KLM Labs., Inc.*, 984 F.2d 1182, 1189-90 (Fed. Cir. 1993) (holding on summary judgment that "[s]moking gun evidence is not required in order to establish an intent to deceive") (internal quotations omitted). This is particularly true where, as here, the applicant offers no "credible

explanation" for its or its employees withholding of material information. *Bruno*, 394 F.3d at 1354. In such cases, "an intent to deceive is generally inferred from the facts and circumstances ... ." *Id.* "[W]here withheld information is material and the patentee knew or should have know[n] of that materiality, he or she can expect to have great difficulty in establishing subjective good faith sufficient to overcome an inference of intent to mislead." *Bristol-Myers*, 326 F.3d at 1239. In this case, circumstantial evidence as well as the testimony of GSK's named inventor—not just GSK's failure to offer a credible explanation for withholding such information—provides the Court with ample basis to infer intent, as discussed below.

IV. ARGUMENT

Inequitable conduct is an equitable defense to an assertion of patent infringement. *See Nobelpharma*, 141 F.3d at 1070. The defense arises from the duties owed by applicants to the USPTO during the *ex parte* prosecution of patent applications. Because of the limited resources of the USPTO, and the lack of any adversarial process, the USPTO must be able to rely on an applicant's good faith and candor during patent prosecution. *Molins PLC*, 48 F.3d at 1178. A breach of those duties—whether in the form of withheld prior art, false or misleading representations, failure to identify proper inventors, failure to disclose the interests of declarants, even misstatements regarding payment of fees—may result in the patent being deemed unenforceable even if the breach would not independently result in invalidity. *See id.* at 1179-80 ("Nor is a reference immaterial simply because the claims are eventually deemed by an examiner to be patentable thereover.").

A. The '860 Patent Should Be Held Unenforceable For False Claims Of Inventorship.

Proper inventorship is a prerequisite to patentability and the deliberate failure to properly name inventors has previously been deemed inequitable conduct. *PerSeptive*, 225 F.3d at 1321-

22. Here, the '860 patent should be held unenforceable for failure to disclose the proper inventors of the '860 patent and failure to disclose material prior art relating to those inventors. Intentional failure to disclose proper inventorship is grounds for inequitable conduct. *Id.* The evidence in this case clearly and convincingly shows Dr. Owen was not, as he declared, the sole inventor of the claimed subject matter and that, to the extent there was any patentable subject matter in the '860 patent, it was invented by others.

1. Dr. Owen Falsely Claimed To Be The "Sole Inventor" Of The Method Of Using Ropinirole As An Anti-Parkinson's Drug.

To the extent there was anything patentable about the use of ropinirole hydrochloride for treating Parkinson's disease, the inventor was not Dr. Owen. "The 'inventor,' in patent law, is the person or persons who conceived the patented invention." *C.R. Bard, Inc. v. M3 Sys., Inc.*, 157 F.3d 1340, 1352 (Fed. Cir. 1998). "Conception is the 'formation in the mind of the inventor, of a definite and permanent idea of the complete and operative invention, as it is hereafter to be applied in practice.'" *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). "Conception is complete when the idea is so clearly defined in the inventor's mind that only ordinary skill would be necessary to reduce the invention to practice, without extensive research or experimentation." *Burroughs Wellcome Co. v. Barr Labs., Inc.*, 40 F.3d 1223, 1228 (Fed. Cir. 1994).

Here, Dr. Owen's sworn declaration statement claiming that he was the "sole inventor" of the inventions claimed in the '860 patent (DTX 97) was false and misleading in two ways. ***First***, the "hypothesis" that Dr. Owen allegedly developed based on the observation of CNS effects in Ms. Wright's rat experiments (Owen Dep. Tr. 114:21-115:15) was not a "definite and permanent idea" that ropinirole could be used to treat Parkinson's disease, so he did not invent even that portion of the claimed methods. ***Second***, Dr. Owen emphatically denied having ever thought

about whether any of the other 749 compounds identified in claim 1 would work as treatments for Parkinson's disease; instead, his work was "focused entirely on ropinirole." (*Id.* at 120:7-14; 18-22.) So he could not have been the sole inventor of claim 1. *See In re Mantell*, 454 F.2d at 1402; *Bosies*, 27 F.3d at 542-43.

a. Dr. Owen was not the first person to form a "definite and permanent idea" that ropinirole could be used to treat Parkinson's disease.

At trial, GSK contended that merely knowing that a compound was a centrally acting D_2 agonist was not enough to give a person of ordinary skill in the relevant field a reasonable expectation that the compound was a potential anti-Parkinson's agent. (Trial Tr. at 603:17-604:4.) Yet this is the only thing that Dr. Owen claims to have contributed to the conception of the inventions claimed in the '860 patent. (Owen Dep. Tr. at 114:21-115:15.) To the extent the Court accepts GSK's invalidity position, the inventors of claim 1 of the '860 patent were the University of Bradford researchers, including Dr. Costall, who first conducted experiments directed to determining whether ropinirole exhibited anti-Parkinson's activity. (*Id.* at 110:10-111:3.) Indeed, the cornerstone of Dr. Owen's hypothesis—Ms. Wright's incidental observation of stereotypy in rats given ropinirole—was undercut by the further testing of the Bradford researchers, as reported in the '860 patent itself. ('860 patent, col. 4, ll. 28-30 ("At doses of 1.0, 10.0 and 100 mg/kg i.p. Compound A caused no dose dependent stereotypies in the mouse or rat ... .").) This discrepancy confirms the work required to turn Dr. Owen's "hypothesis" into a definite and permanent idea of how ropinirole worked to treat Parkinson's disease. The experiments run by these "experts" were far from routine work for a person of ordinary skill in the art—indeed, GSK went to the University of Bradford because it lacked the expertise to do these experiments by itself. As a result, Dr. Owen's "hypothesis" was little more than a "prospective hope" that ropinirole would exhibit anti-Parkinson's activity. *See Burroughs*

Wellcome, 40 F.3d at 1229 ("A conception is not complete if the subsequent course of experimentation, especially experimental failures, reveals uncertainty that so undermines the specificity of the inventor's idea that it is not yet a definite and permanent reflection of the complete invention as it will be used in practice."). Where, as here, the claims recite a specific biological result—treatment of Parkinson's disease—it is well-established that the mere hope of obtaining that result was insufficient to qualify as conception of the claimed invention. *See Hitzeman v. Rutter*, 243 F.3d 1345, 1356-57 (Fed. Cir. 2001) (finding "the critical deficiency is that [the putative inventor] specifically claimed the result of a biological process ... with no more than a hope" the result would be achieved and that "[s]uch a bare hope is insufficient to establish conception."); *Alpert v. Slatin*, 305 F.2d 891, 894 (C.C.P.A. 1962) ("If after the claimed conception date extensive research was found necessary before achieving minimum satisfactory performance, obviously the mental embodiment of that date was a mere hope or expectation, a statement of a problem, but not an inventive conception."). And unlike the circumstances in *Burroughs Wellcome*, where the inventors had produced a draft application evidencing their conception before seeking the aid of others to test their ideas, *id.* at 1230, in this case, there is not a single document that attributes the idea of using ropinirole to treat Parkinson's disease to Dr. Owen, while several GSK documents attribute that idea to the Bradford researchers. *See Amax*, 514 F.2d at 1049 (lack of documentation linking putative inventor to claimed process was evidence of no conception).

The University of Bradford researchers selected, performed, and interpreted the tests showing ropinirole hydrochloride was an effective anti-Parkinson's agent and reported their results to Dr. Owen. (DTX 35; Owen Dep. Tr. at 110:10-20.) These tests and results are those disclosed in the '860 patent. (*Id.* at 221:11-15.) Dr. Owen did not run or oversee these tests.

(*Id.* at 110:10-20.) Dr. Owen was not even involved with the ropinirole project when the final test data was provided to GSK—Mr. Eden had taken his place by then. (*Id.* at 218:7-219:5; DTX 36; DTX 37.) Thus, if merely knowing a compound is a centrally active D_2 agonist is not a sufficient basis to reasonably expect that the compound will also have anti-Parkinson's potential—as GSK contended at trial—then the Bradford researchers are at least co-inventors, if not the sole inventors, of claim 1 of the '860 patent.

On the other hand, if the idea that ropinirole will exhibit anti-Parkinson's activity is inherent in the discovery that it acts centrally, then the '860 patent fails to identify Ms. Annette Wright as a sole or joint inventor. It was Ms. Wright who is credited by GSK as discovering that ropinirole had central effects. (Eden Dep. Tr. at 62:4-8.) Ms. Wright ran the tests and wrote them up in her lab notebook. (DTX 24.) She discussed her findings with Mr. Eden. (Eden Dep. Tr. at 74:20-75:1.) By all accounts, no one at GSK, including Ms. Wright, expected to find central effects when she ran her tests. (Harvey Dep. Tr. at 48:4-6; 48:13-15.) Accordingly, if the "invention" of the '860 patent is the discovery that ropinirole acts centrally, Ms. Wright, not Dr. Owen, is a proper co-inventor, if not the sole inventor.

b. Dr. Owen did not invent any method of treatment using the other 749 compounds identified in claim 1 of the '860 patent.

The evidence also clearly shows Dr. Owen did not invent the subject matter of claim 1 of the '860 patent. Claim 1, which GSK originally asserted against Teva but dropped after Dr. Owen's deposition, covers a method of treating Parkinson's disease using at least 750 different compounds. ('860 patent, col. 1, ll. 48-53; col. 2, ll. 4-24.) To be the sole inventor of the '860 patent, Dr. Owen also had to have conceived of the use of the 749 compounds other than ropinirole identified in claim 1 as treatments for Parkinson's disease. *See In re Mantell*, 454 F.2d at 1402; *Bosies*, 27 F.3d at 542-43.

Dr. Owen was emphatic that he only considered using ropinirole hydrochloride in the claimed methods. (*See, e.g.*, Owen Dep. Tr. at 120:7-14; 120:18-22; 131:13-19) He testified that he would have no expectation that the other 749 compounds recited in claim 1 would work to treat Parkinson's disease absent testing of the type described in his patent. (*Id.* at 134:1-10.) And he testified he did not know the origin of the 749 other compounds included in claim 1. (*Id.* at 121:1-7; 121:13-16.) Thanks to the deception of Dr. Owen and the others who prepared and prosecuted the '860 patent, neither did the USPTO. Indeed, GSK has been unable or unwilling to reveal that information to this day.

Not all of the other compounds recited in claim 1 of the '860 patent came from the '808 patent. (Trial Tr. at 517:23-518:1.) Rather, someone—not Dr. Owen—selected compounds from undisclosed sources other than the '808 patent. Presumably there was some basis for claiming that these additional, untested compounds are useful in treating Parkinson's disease, but no rationale is provided in the '860 patent. If there is anything patentable about the use of these compounds for treating Parkinson's disease, someone other than Dr. Owen discovered it.

Similarly, some, but not all, of the compounds in the '808 patent were included in claim 1. (*Id.* at 515:1-10.) Someone—again, not Dr. Owen—selected a very limited subset of compounds from the thousands of compounds disclosed in the '808 patent. Presumably there was some basis for excluding a substantial number of the D_2 agonist compounds in the '808 patent from the scope of claim 1 of the '860 patent. Again, the '860 patent provides no rationale for the exclusion nor information about who made this selection. What is clear is that Dr. Owen did not make these decisions. Rather, he viewed himself incompetent to make such judgments about the chemical nature of the compounds. (Owen Dep. Tr. at 131:20-132:3; 132:5-12.)

Someone other than Dr. Owen selected certain additional related compounds to include within claim 1, while excluding others. This person should have been a named inventor subject to the same legal duties of candor and disclosure to the USPTO, particularly since the compound selection process employed for claim 1 is, as shown below, highly material to the patentability of the claim.

2. The False Inventorship Claims Were Material To The Patentability Of The '860 Patent.

Inventorship is always material because it is a prerequisite to patentability. *PerSeptive*, 225 F.3d at 1321-22 ("As a critical requirement for obtaining a patent, inventorship is material."). Patents are only issued to the original inventors. 35 U.S.C. § 102(f); Chisum on Patents § 2.01. "Examiners are required to reject applications under 35 U.S.C. § 102(f) on the basis of improper inventorship." *PerSeptive*, 225 F.3d at 1321. Inventorship is material not only because Congress says so, but also because it is the inventors who bear the duties of disclosure and candor to the USPTO. *Molins PLC*, 48 F.3d at 1178. Because an examiner "must attend to the question of inventorship," pursuant to 35 U.S.C. § 102(f), omissions or misrepresentations regarding the inventorship of a patent is material. *PerSeptive*, 225 F.3d at 1322.

The failure to disclose the University of Bradford inventors is self-evidently material. The University of Bradford researchers performed the relevant tests that are described in the patent as supporting the claim that ropinirole hydrochloride is an effective treatment for Parkinson's disease. (Owen Dep. Tr. at 221:11-15.) Moreover, the University of Bradford researchers memorialized their findings in a series of reports that were provided to GSK. (*See, e.g.*, DTX 35 at GSK-REQ001030-31.) Those reports that were provided to GSK before the filing of the '860 patent are prior art to the '860 patent application under 35 U.S.C. § 102(f). Even confidential reports that are not available to the public can be prior art under § 102(f).

OddzOn Prods., Inc. v. Just Toys, Inc., 122 F.3d 1396, 1401-02 (Fed. Cir. 1997). These reports anticipate the subject matter of claim 3 since they describe ropinirole as effective for treating Parkinson's disease. (DTX 35 at GSK-REQ001030 ("This is evidence of marked dopamine agonist action for SK&F 101468-A [*i.e.*, ropinirole] in the striatum which would support a potential value in the treatment of Parkinson's disease."); at GSK-REQ001031 ("It would be reasonable to further investigate the actions of SK&F 101468-A, or a related compound, as an antiparkinson agent ....").) Anticipating prior art is the most material form of prior art. *Fox Indus., Inc. v. Structural Preservation Sys., Inc.*, 922 F.2d 801, 804 (Fed. Cir. 1990). Thus, the failure to identify the proper inventors, and their work, is an omission of the highest possible materiality.

The failure to disclose Annette Wright's contributions is likewise material. To the extent claim 1 is deemed to be patentable over the '808 patent because of unexpected activity in the brain, it was Ms. Wright, not Dr. Owen, who made this discovery. (*See* Eden Dep. Tr. at 62:4-8; DTX 24.) The '860 patent states that the central effects Ms. Wright first observed would have been unexpected by those of ordinary skill in the art and distinguishes the prior art '808 patent on that basis by citing an article by GSK's own researchers. (*See* '860 patent.) Thus, the '860 patent itself emphasizes that Ms. Wright's contribution to conception was key to conception of the claimed methods over contradictory information in the prior art.

Finally, the failure to name the inventor of the other 749 compounds was highly material. Some of the compounds claimed in claim 1 of the '860 patent would not be expected to work. (Trial Tr. at 523:4-11.) In fact, at least one of the compounds that was anonymously selected for inclusion in claim 1 had already been shown by GSK in prior art articles to be dopaminergically inactive. (DTX 56; DTX 376.) There can be no more material information than identifying the

person and rationale for identifying compounds as treatments for Parkinson's disease in claim 1 that GSK had already reported in public literature to be inactive. Because a claim must be enabled (35 U.S.C. §112 ¶ 1), compounds known to be inactive cannot properly be claimed in a patent as active. *See Bristol-Myers*, 326 F.3d at 1236-37 (failure to disclose article identifying inoperative embodiments of claimed invention constituted inequitable conduct). The inclusion of subject matter that is known to be inactive can itself constitute inequitable conduct.

3. The Statements Were Made With The Intent To Deceive The USPTO.

The failure to identify the proper inventors was no oversight. Rather, it was purposeful and intentional. There is no logical explanation for how Dr. Owen can claim to be the sole inventor of 749 compounds that he never considered using to treat Parkinson's disease. Indeed, Dr. Owen admitted he had no idea where the generic structure in claim 1 came from other than to guess that GSK's patent attorneys had conjured it up. (Owen Dep. Tr. at 131:20-132:3; 132:5-16.) There is also no logical explanation for how Dr. Owen can claim to be the person who discovered ropinirole hydrochloride was an effective anti-Parkinson's drug when all of the tests relied on in the patent in support of this claim were performed by someone else.

There are, however, compelling reasons why the missing inventors were not disclosed. If the University of Bradford professors were the real inventors, then GSK may not have exclusive rights, or potentially any rights, to the use of ropinirole to treat Parkinson's disease. *See Ethicon, Inc. v. U.S. Surgical Corp.*, 135 F.3d 1456, 1465 (Fed. Cir. 1998) ("[I]n the context of joint inventorship, each co-inventor presumptively owns a pro rata undivided interest in the entire patent, no matter what their respective contributions.") (footnote omitted). GSK admits that a lawyer was assigned to the ropinirole project team to seek ways to increase the scope of their patent protection and patent "opportunities" (Harvey Dep. Tr. 151:10-17), so GSK has

motivation to omit inventors not under its control to maximize its ownership interest in the invention.

Similarly, if Dr. Owen and GSK's attorneys had identified the inventor of the hundreds of other compounds in claim 1, GSK would have had to disclose additional information, including prior art. As GSK was already aware, among the compounds recited in claim 1 as effective anti-Parkinson's treatments were compounds that were described as inactive in GSK's own articles. (*See* DTX 56.) In addition, Professor Costall—the head of the team of Bradford researchers that performed all the tests to show ropinirole's effectiveness in treating Parkinson's disease—had previously published an article suggesting that several compounds in claim 1 (having a dibutylamino side chain) could not be used to treat Parkinson's disease. (Trial Tr. at 227:6-229:1; DTX 160.) The fact that compounds claimed to be active in the '860 patent were, in fact, inactive undermines the entire premise of claim 1 whereby GSK sought to obtain expansive patent protection over hundreds of compounds based solely on data from one, ropinirole hydrochloride. By naming Dr. Owen, who knew nothing about the other compounds or their pharmacological properties, as the only inventor of the '860 patent, GSK attained its goal of expansive patent coverage while avoiding the disclosure of potentially invalidating prior art of which the actual inventors were aware.

B. The '860 Patent Should Be Held Unenforceable For False and Misleading Statements Made To Overcome The Prior Art.

Separate and apart from the failure to disclose the proper inventors of the '860 patent and the failure to disclose material prior art relating to those unnamed inventors, the '860 patent should be held unenforceable for false and misleading statements made to the USPTO. Even GSK cannot dispute that making false and misleading statements during prosecution is a breach of the duty of candor to the USPTO. *See Hoffman-LaRoche*, 323 F.3d at 1371. Here, clear and

convincing evidence shows that the key representations made in the '860 patent to distinguish the prior art D_2 agonists were false and misleading, and that the representations were intentionally made by Dr. Owen and his representatives to obtain additional patent protection for ropinirole as an anti-Parkinson's agent beyond that provided in the '808 patent.

1. The Statements Creating the Pre- / Post-Synaptic Distinction Were False and Misleading.

During the prosecution of the '860 patent application, Dr. Owen and GSK's patent attorneys characterized the prior art dopamine agonists known to be effective anti-Parkinson's drugs as "post-synaptic" D_2 agonists. ('860 patent, col. 1, ll. 36-38.) Conversely, they told the public and the USPTO that the compounds they now sought to patent as treatments for Parkinson's disease had previously been known in the art as only "presynaptic" D_2 agonists. (*Id.* at col. 1, ll. 48-53.) The '860 patent then attributes to Dr. Owen the discovery that these compounds were also "post synaptic" D_2 agonists that were active in the brain. (*Id.*) On the basis of this allegedly new discovery, the patent concluded that the claimed compounds would be "expected to have utility in the treatment of Parkinsonism." (*Id.*) These representations in the '860 patent were false and misleading.

While the '860 patent says the prior art Parkinson's disease treatments were known as "post-synaptic" D_2 agonists (*See id.*), GSK's own prior art article—the DeMarinis article—contradicts that statement (DTX 56). The DeMarinis article describes these same prior art D_2 agonists as pre-synaptic D_2 agonists (*Id.*) In other words, the distinction between pre- versus post-synaptic D_2 agonists that is drawn in the '860 patent to distinguish the prior art is false.

GSK itself has admitted that this statement in the DeMarinis article was at-odds with the '860 patent's characterization of the prior art compounds. The European Patent Office ("EPO") initially rejected the European counterpart to the '860 patent based on this discrepancy between

what the DeMarinis article stated about the site of action of the prior art compounds and the characterization of those compounds in the '860 patent. (DTX 134.) To overcome the EPO's rejection, GSK was forced to acknowledge that statements in the European application—which were identical to the '860 patent's statements characterizing the same prior art treatments for Parkinson's disease—were, in fact, "an error." (DTX 133 at GSK-REQ018298.) Put another way, the EPO caught GSK's deception, and GSK acknowledged the statements were false. Although the '860 patent had already issued by that time, at no time did GSK attempt to correct the '860 patent through reissue or otherwise.

Worse yet, Dr. Owen knew the pre-/post-synaptic distinction drawn in the '860 patent was false. Dr. Owen himself understood there was no pharmacological distinction between "pre-" and "post-" synaptic receptors—"[i]f it's an agonist for D_2 receptors, it will be an agonist for D_2 receptors, and whether they are presynaptic or postsynaptic is a piece of anatomy, not a piece of pharmacology." (Owen Dep. Tr. at 191:11-14.) Far from being the critical distinction it is portrayed to be in the '860 patent, Dr. Owen admitted the distinction was "an absolute irrelevance." (*Id.* at 192:19-193:3.)

2. These Statements Were Material To Patentability.

The test for materiality is whether "there is a substantial likelihood that a reasonable examiner would have considered the information important in deciding whether to allow the application to issue as a patent." *Ferring*, 437 F.3d at 1187 (quoting 37 C.F.R. § 1.56 (1989)). Here, the false statements regarding pre- versus post-synaptic receptors are highly material to the patentability of the '860 patent. In fact, it is central to the patentability of all of the claims.

The patent acknowledges the basic scientific principle that post-synaptic D_2 receptors that are active in the brain would be "expected to have utility in the treatment of Parkinsonism" ('860 patent, col. 1, ll. 52-3.) The prior art '808 patent clearly disclosed that its compounds—

including ropinirole hydrochloride—were D_2 agonists. ('808 patent, col. 4, ll. 31-34.) There was therefore little to distinguish the D_2 agonists in the '860 patent from the D_2 agonists known in the prior art as useful for treating Parkinson's disease. Thus, to obtain the '860 patent, Dr. Owen and GSK misrepresented in the patent specification that the compounds disclosed in the '808 patent were only known to be "presynaptic" D_2 agonists that were not known to be active in the brain and that the prior art anti-Parkinson's agents were only known as "post synaptic" D_2 agonists. ('860 patent, col. 1, ll. 48-53.) But as Dr. Owen candidly acknowledges, the distinction between pre- and post-synaptic receptors is "an absolute irrelevance." (Owen Dep. Tr. at 192:19-193:3.) Had the USPTO known the truth, the '860 patent may never have issued, and GSK's patent protection would have been limited to the prior art '808 patent.

The EPO resolved any doubts about the high materiality of the distinction made by the '860 patent. Indeed, the EPO rejected the claims of the European counterpart application based on the same contradiction in the DeMarinis article. (DTX 134 at GSK-REQ018296-97.) Although the European Patent Office ultimately issued the application after additional arguments by GSK attorneys, the rejection plainly indicates the high materiality placed on the "pre-" versus "post-" synaptic receptor representations in the patent application. *See Dayco Prods., Inc. v. Total Containment, Inc.*, 329 F.3d 1358, 1368 (Fed. Cir. 2003) ("An adverse decision by another examiner, therefore, meets the materiality standard."); *Molins PLC,* 48 F.3d at 1182 (finding that "[f]ailure to cite to the PTO a material reference cited elsewhere in the world justifies a strong inference that the withholding was intentional" and that the nondisclosure amounted to inequitable conduct.).

3. The Statements Were Made With The Intent to Deceive The USPTO.

The evidence shows the false and misleading statements were made intentionally. Dr. Owen swore to the USPTO that he read and understood his patent application. (*See* DTX 97.) If

that is true, he read and understood that false and misleading representations were being made to the USPTO in order to distinguish the prior art and to obtain extended patent coverage. If he did not, in fact, read and understand his application, then he lied in his declaration to the USPTO. In either case, intentional and material misrepresentations were made to the USPTO.

Similarly, the evidence shows that those prosecuting the patent application were aware of the false nature of the representations. The prior art DeMarinis article contradicts the very distinctions made in the '860 patent. And the evidence shows that Dr. Owen and GSK's patent attorneys knew of the DeMarinis article while they were prosecuting the '860 patent. (*See, e.g.*, DTX 311 at GSK-REQ006762.) *See Brasseler, U.S.A. I, L.P. v. Stryker Sales Corp.*, 267 F.3d 1370, 1383 (Fed. Cir. 2001) ("'[O]ne should not be able to cultivate ignorance . . . merely to avoid actual knowledge of that information or prior art.' Where one does, deceptive intent may be inferred.") (citation omitted).

The DeMarinis article is about the pharmacological properties of the same ropinirole hydrochloride compound that is the subject of the '860 patent application. (DTX 56.) It is written by many of the same GSK researchers involved in the ropinirole project that is the basis of the '860 patent application. (*See id.*) And it was written and published at approximately the same time—1986—that Dr. Owen was involved in the ropinirole hydrochloride project. (*See id.*) In fact, in 1989, while the '860 patent application was still pending at the USPTO, Dr. Owen and a number of other GSK researchers co-authored a book chapter that cited the DeMarinis article as a reference. (DTX 311 at GSK-REQ094405 at reference no. 28.) The book chapter was included within the internal prosecution files maintained by GSK's patent attorneys for the '808 patent, further demonstrating that GSK's attorneys were aware of Dr. Owen's knowledge of the DeMarinis article. (*Id.*) And the DeMarinis article itself was included in GSK's internal

prosecution file for the '860 patent (DTX 312 at GSK-REQ094559), so GSK's patent attorneys should have disclosed the article based on their own duties to the USPTO.

The evidence shows that the false and misleading statements were not "inadvertent" mistakes. They were made by people substantively involved in the prosecution of the '860 patent who knew better, but deemed the value of obtaining additional years of patent protection outweighed the odds that their deception would be caught and result in an unenforceable patent. *See Molins PLC*, 48 F.3d at 1181 (holding a patent unenforceable for inequitable conduct where a "seasoned patent practitioner… knew of a highly material reference but did not cite it").

V. GSK CANNOT EXPLAIN AWAY ITS INEQUITABLE CONDUCT.

In its pre-trial submissions and arguments, GSK focused on two excuses for its inequitable conduct. Neither is legally or logically sound.

First, GSK argues that inequitable conduct does not matter here because it relates to claim 1, which it does not now assert. This is wrong for several reasons. As an initial matter, Teva's inequitable conduct arguments, as explained both above and in its pre-trial submissions, were not limited to claim 1—only GSK's inequitable conduct in failing to name the inventor of the 749 claimed compounds other than ropinirole is unique to claim 1. More importantly, however, whether the claim is asserted or not is irrelevant for purposes of inequitable conduct. *See Pharmacia Corp. v. Par Pharm., Inc.*, 417 F.3d 1369, 1374-75 (Fed. Cir. 2005) ("This court has held that a finding of inequitable conduct in the acquisition of even a single claim of a patent renders the remaining claims of that patent unenforceable, even those without the taint of inequitable conduct."); *Kingsdown Med. Consultants, Ltd. v. Hollister, Inc.*, 863 F.2d 867, 877 (Fed. Cir. 1988) (en banc in pertinent part) ("When a court has finally determined that inequitable conduct occurred in relation to one or more claims during prosecution of the patent application, the entire patent is rendered unenforceable."). A party cannot avoid the

consequences of its inequitable conduct by picking and choosing the claims it wishes to assert in litigation. In fact, a patent may be held unenforceable for inequitable conduct on the basis of inequitable conduct that occurred in an entirely different (but related) patent. *See, e.g.*, *Consolidated Aluminum v. Foseco Int'l Ltd.*, 910 F.2d 804, 812 (Fed. Cir. 1990). Finally, it bears emphasis that GSK ***did*** assert claim 1 of the '860 patent against Teva. (DTX 140 at Pl.'s Response to Teva's Interrogatory No. 1.) GSK only chose to drop claim 1 after Dr. Owen testified at his deposition that he had no knowledge of the 749 compounds other than ropinirole identified in the claim.

Second, GSK argues that the circumstances surrounding the acts of alleged inequitable conduct are an indictment of the patent prosecution process. This is likewise nonsense. Inventors and those involved on their behalf in preparing and prosecuting patent applications owe strict duties of "candor, good faith, and honesty" to the USPTO. *Bristol-Myers*, 326 F.3d at 1233. Filing patent applications that represent facts known by the applicant(s) to be false is not an accepted patent prosecution process. Filing patent applications that take credit for others' inventions is not an accepted patent prosecution process. Seeking patent protection on allegedly active compounds that are (1) unknown and never considered by the inventor but which (2) are known to be inactive, is not an accepted patent prosecution process. And filing a declaration with the USPTO making averments that are false is not an accepted patent prosecution process. These are examples of inequitable conduct that apply to this specific case, and GSK has offered no evidence related to this specific case to rebut the *prima facie* case of inequitable conduct laid out in the record.

VI. CONCLUSION

For the above stated reasons, Teva respectfully asks the court to find the '860 patent unenforceable due to inequitable conduct.

Respectfully submitted,

John W. Shaw (No. 3362)
Monté T. Squire (No. 4764)
YOUNG CONAWAY STARGATT & TAYLOR, LLP
The Brandywine Building
1000 West Street, 17th Floor
Wilmington, DE 19801
Telephone: (302) 571-6600
msquire@ycst.com

Attorneys for Defendant
Teva Pharmaceuticals USA, Inc.

Of Counsel
Daniel F. Attridge, P.C.
Edward C. Donovan
Andrew B. Kay
Charanjit Brahma
Corey J. Manley
Valerie L. Gutmann
KIRKLAND & ELLIS LLP
655 Fifteenth St., N.W.
Suite 1200
Washington, D.C. 20005
Telephone: (202) 879-5000

Dated: February 7, 2007

CERTIFICATE OF SERVICE

I, Monté T. Squire, Esquire, hereby certify that on February 14, 2007, I caused to be electronically filed a true and correct copy of the foregoing document with the Clerk of the Court using CM/ECF, which will send notification that such filing is available for viewing and downloading to the following counsel of record:

Patricia Smink Rogowski, Esquire
Connolly, Bove, Lodge & Hutz LLP
The Nemours Building
1007 North Orange Street
Wilmington, DE 19801

I further certify that on February 14, 2007, I caused a copy of the foregoing document to be served by hand delivery on the above-listed counsel of record and the following non-registered participants in the manner indicated:

BY E-MAIL

William F. Lee, Esquire
Wilmer, Cutler, Pickering, Hale and Dorr LLP
60 State Street
Boston, MA 02109

Cristina C. Ashworth, Esquire
Wilmer, Cutler, Pickering, Hale and Dorr LLP
1875 Pennsylvania Avenue, N.W.
Washington, DC 20006

YOUNG CONAWAY STARGATT & TAYLOR, LLP

/s/ *Monté T. Squire*
Monté T. Squire (No. 4764)
The Brandywine Building
1000 West Street, 17th Floor
Wilmington, Delaware 19801
(302) 571-6600
msquire@ycst.com

Attorneys for Teva Pharmaceuticals U.S.A., Inc.